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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,698	02/03/2005	Yasuyoshi Ueda	21581-00490-US	2912

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CONNOLLY BOVE LODGE & HUTZ LLP
1875 EYE STREET, N.W.
SUITE 1100
WASHINGTON, DC 20006

EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	**PAPER NUMBER**
1657	

MAIL DATE	DELIVERY MODE
12/04/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,698	UEDA ET AL.	
	Examiner	Art Unit	
	SATYENDRA SINGH	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

5a) Of the above claim(s) *1,2,4,8,12,13,15,17,20 and 28* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *29,31,34,36,39-41,46,49,51,64,66,69-71,73-77 and 79-81* is/are rejected.

8)☒ Claim(s) *72* is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,4,8,12,13,15,17,20,28,29,31,34,36,39-41,46,49,51,64,66,69-77 and 79-81.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on **06/13/2012** (along with 1.132 declaration from inventor, **Takahiro Ueda**) has been entered.

Claim 67 have been canceled by applicants.

Claim 81 has been newly presented.

Claims 1, 2, 4, 8, 12, 13, 15, 17, 20, 28, 29, 31, 34, 36, 39-41, 46, 49, 51, 64, 66, 69-77, and 79-81, as currently amended, are pending in this application.

Claims 1, 2, 4, 8, 12, 13, 15, 17, 20 and 28 remain withdrawn.

Claims 29, 31, 34, 36, 39-41, 46, 49, 51, 64, 66, 69-77 and 79-81 (the elected invention of group III, as currently amended) are examined on their merits in this office action.

Claim Rejections - 35 USC § 103- Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. **Claims 29, 31, 34, 36, 39-41, 46, 49, 51, 64, 66, 69-71, 73-77 and 79-81** (as currently amended) **are/remain** rejected under 35 U.S.C. 103(a) as being unpatentable over Chopra (WIPO document, WO 01/52822 A1) taken with Motoyama et al (US 4,751,241; 1988; previously cited by the examiner).

Claims (as currently presented) are directed to "a reduced coenzyme Q10-containing composition which **comprises** reduced coenzyme Q10 (amount not specified in the instant claim), a polyglycerol fatty acid ester, and at least one member selected from the group consisting of a fat component, an oil component and a polyol,

wherein a content of the at least one member selected from the group consisting of a fat component, an oil component and a polyol is not lower than 50% by weight based on total weight of the composition minus a weight of coenzyme Q10; a content of the polyglycerol fatty acid ester is not lower than 1% by weight and not higher than 40% by weight based on total weight of the composition minus a weight of coenzyme Q10;

a content of Tween and/or Span species, *when the same is further contained* in the composition, is not higher than 30% by weight based on total weight of the composition minus a weight of coenzyme Q10; and wherein the fat component or oil component is at least one member selected from the group consisting of coconut oil, palm oil, palm kernel oil, linseed oil, camellia oil, brown rice germ oil, avocado oil, rapeseed oil, rice oil, peanut oil, corn oil, wheat germ oil, soybean oil, perilla oil, cottonseed oil, sunflower seed oil, kapok oil, evening primrose oil, shea butter, sal fat, cacao butter, sesame oil, safflower oil, olive oil, lard, milk fat, fish oil beef tallow, modified fat component, modified oil component, medium-chain fatty acid triglycerides, fatty acid partial glycerides, and phospholipids, wherein the modified fat component or modified oil component is derived from at least one member selected from the group consisting of coconut oil, palm oil, palm kernel oil, linseed oil, camellia oil, brown rice germ oil, avocado oil, rapeseed oil, rice oil, peanut oil, corn oil, wheat germ oil, soybean oil, perilla oil, cottonseed oil, sunflower seed oil, kapok oil, evening primrose oil, shea butter, sal fat, cacao butter, sesame oil, safflower oil, olive oil, lard, milk fat, fish oil, and beef tallow by a

process selected from the group consisting of fractionation, hydrogenation and transesterification; and

wherein a percent retention of reduced coenzyme Q10 after 3 days storage in the air at 40°C under a light-shielded condition is not lower than 70%, with the percent retention in the corresponding composition composed of reduced coenzyme Q10, and at least one member selected from the group consisting of the fat component, the oil component and the polyol alone after storage under the same conditions being taken as 100%." (see instant claim 29, in particular).

(see also limitations of instant claims 31, 34, 36, 39-41, 46, 49, 51, 64, 66, 69-77, 79 and 80).

The **newly added claim 81** is directed to "the composition according to Claim 29, wherein the content of reduced coenzyme Q10 in the composition is *not higher than 30%* by weight."

Chopra (IDS) discloses a reduced coenzyme Q10-containing composition (see abstract, claims, and examples I-X, in particular) comprising reduced coenzyme Q10, a fat or oil, and a polyol (such as glycerol or other polyhydric alcohols). Chopra discloses reduced coenzyme Q10-containing compositions in various forms including oral dosage forms such as soft capsules, etc. which are "substantially ubiquinone-free" (i.e. the oxidized form of coenzyme Q10), and incorporate reducing agents, oils or fat, polyols, and one or more surfactants (see WIPO document, page 14, 5th paragraph, and examples I-X, in particular). Chopra discloses that such Co-Q10 (**in an amount from 0.1% to 10% by weight**; see Chopra, page 7, and ranges disclosed for examples III and IV, in particular) containing compositions may comprise components such as soybean oil, sunflower oil, safflower oil, rapeseed oil, fish oil, medium chain triglycerides, phospholipids (as recited in instant claim 62; see Chopra, page 12, last paragraph and various embodiments), surfactants (such as **Tween 80**, 20-90%; or Span 80, 1-15%; see examples I, III, IV, VI, in particular), reducing agent such as vitamin C or ascorbyl palmitate (see Chopra, examples, and claim 2, in particular), **vitamin E acetate, D-alpha tocopherol, or esters thereof**

(in an amount of 2-20%; see page 8, examples II, IV and X, in particular) and can be prepared or stored in a deoxygenated (such as prepared and sealed under nitrogen gas; see Chopra, page 21, example I, last paragraph, in particular).

However, a reduced coenzyme Q10-containing composition comprising **polyglycerol fatty acid ester** (as specifically recited in instant claims 70-71), and "wherein a content of the polyglycerol fatty acid ester is not lower than 1% by weight and not higher than 40% by weight based on total weight of the composition minus a weight of coenzyme Q10" (see instant claim 29), is not explicitly taught by the compositions disclosed by Chopra.

Motoyama et al (1988) discloses **polyglycerol fatty acid esters** (see abstract, summary of the invention, columns 1-2, in particular) such as triglycerol monooleate, diglycerol monolinolenate, diglycerol monooleate, etc. (see column 2, lines 23-30, in particular) to be used as emulsifying agents for drugs that are very slightly soluble in water (including ubiquinones, CoQ10; see column 2, lines 38-56, in particular; and also suitable for compositions comprising lipid-soluble reducing agents and/or nutrients such as vitamin E rich natural oils, shark liver oil, etc.) in order to enhance the absorption and thus bioavailability of said drugs (i.e. in a pharmaceutical composition) in the digestive tract when administered using oral dosage forms such as soft capsules (see columns 4-5, and examples), and wherein the content of polyglycerol fatty acid ester used in the composition for increasing the dispersibility of the drug is usually 0.05~30 parts by weight for one part by weight of the drug (see column 4, lines 53-56, and last paragraph; and examples, in particular).

Therefore, it would have been obvious to a person of ordinary skill in the pharmaceutical composition art to modify the reduced coenzyme Q10-containing composition of Chopra such

that it contains (in addition to the surfactants such as Tween or Span) an emulsifying agent such as polyglycerol fatty acid ester as explicitly taught and exemplified by Motoyama et al.

One of ordinary skill in the art would have been motivated at the time of invention to make such modification in the composition taught by Chopra in order to obtain a better reduced coenzyme Q10-containing composition (having an enhanced absorption and bioavailability in the mammalian gut) as suggested by Motoyama et al, with a reasonable expectation of success.

The limitations, "wherein the content of the polyglycerol fatty acid ester is not lower than 1% by weight and not higher than 40% by weight based on total weight of the composition minus a weight of coenzyme Q10" would have been obvious to a person of ordinary skill in the art at the time this invention was made as Motoyama et al disclose the suitability of a broad range of concentrations that can be used with a drug that is very slightly soluble in water (such as Co-Q10, and vitamin E containing drugs or nutrients) in order to improve its dispersibility and thus its bioavailability owing to the surface active properties of said polyglycerol fatty acid esters (see column 4, lines 38-42, in particular) when combined with the composition as claimed. The scope of the claimed subject matter, as currently presented by applicants, fails to patentably distinguish over the state of the art as represented by the cited prior art references of record.

With regards to the limitations (i.e. the content of the fat component or oil component or a polyol, on percent basis; claim 29, in particular), claim 36 (the content of ascorbic acid, on percent basis), claim 41 (the content of surfactant), and claim 64 (the content of reduced Co-Q10, on percent basis), it is to be noted that given the detailed disclosures of all the components and their amounts used for various preparations or dosage forms by Chopra and Motoyama et al (as discussed above), the adjustments to the amount and/or the contents and ratio of various

components used in the Q10-containing composition would have been obvious to a person of ordinary skill in the pharmaceutical formulation art in order to achieve a better and stable composition containing reduced Coenzyme Q10.

The limitations of "percent retention of reduced coenzyme Q10" after certain storage period at a desired temperature in the air (see claim 29, current amendment) have been taken as intrinsic feature of the reduced coenzyme Q10 composition as stabilized and disclosed in the art by Chopra when taken with the disclosure of Motoyama et al (for the use of polyglycerol fatty acid ester, diglycerol monooleate as an emulsifier for stabilizing Co-Q10 composition), and would have been obvious and fully contemplated by an artisan of ordinary skill in the art at the time the claimed invention was made. Moreover, claim 29 as currently presented does not recite any specific amount of Co-Q10 in the composition as claimed. Similarly, limitations of instant claims 46, 49, 51 and 69 are taken to be intrinsic to the composition taught by the combined teachings of the cited prior art references of record, as discussed above.

The 103(a) rejection of record is therefore properly made and maintained.

As per MPEP 2144.06, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

As per PPEP 2144.05 (R-3): In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). "[A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." In re Peterson, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003).

As per MPEP 2111.01, during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Response to Applicant's Arguments

Applicant's arguments filed **06/13/2012** (along with the 1.132 declaration by Takahiro Ueda, as they pertain to the prior art rejection of record) have been fully considered but they are not persuasive for the following reasons of record:

Applicant's arguments regarding the unexpected results of the reduced coenzyme Q10-containing composition in the presence of polyglycerol fatty acid ester, diglycerol monooleate as shown in the 1.132 declaration by Takahiro Ueda (see applicant's remarks on pages 9-12, and 132 declaration, experiments 1-2, in particular), is duly noted and fully considered. However, first, it is noted that claim 29 as currently presented does not require any specific amount of the reduced Co-Q10 in the claimed composition. In addition, it is also noted that the claims are not commensurate in scope with the unexpected showings as provided by applicants for the use of one of the many "polyglycerol fatty acid esters" known in the art (see applicant's own disclosure at pages 14-21; and page 21, 2nd paragraph, in particular), such as diglycerol monooleate in the 132 declaration of record (also see the previously filed 132 declaration by Ueda dated 10/29/2010, on page 2, in particular). The scope of the showing must be commensurate with the scope of claims to consider evidence probative of unexpected results, for example. *In re Dill, 202 USPQ 805 (CCPA, 1979), In re Lindner 173 USPQ 356 (CCPA 1972), In re Hyson, 172 USPQ*

399 (CCPA 1972), In re Boesch, 205 USPQ 215, (CCPA 1980), In re Grasselli, 218 USPQ 769 (Fed. Cir. 1983), In re Clemens, 206 USPQ 289 (CCPA 1980). It should be clear that the probative value of the data presented by applicants is not commensurate in scope with the degree of protection sought by the claim (see instant claim 29, for example). In response to applicant's argument (see remarks page 13, 2nd paragraph, in particular) that applicant's reason to combine said polyglycerol fatty acid ester is different, (i.e. for the protection of Co-Q10 from oxidation rather than solubility or stability), the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Since, not all polyglycerol fatty acid esters would necessarily provide the same unexpected results as currently demonstrated for diglycerol monooleate in the 1.132 declaration by applicants, and since applicants have not provided sufficient data/evidence to such effect in the disclosure of record, the obviousness rejection of record over pending claims is properly made/maintained.

Applicants are advised to appropriately amend pending claims (claim 29, in particular) commensurate with the showing of unexpected result in order for further considerations.

Allowable Subject Matter

Claim 72 is objected to as being dependent upon a rejected base claim, but would be considered for allowance (based on applicant's 1.132 declaration for the unexpected results in view of the subject matter of claim 72) if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

NO claims are currently allowed.

This is a continuing examination of applicant's earlier Application No. 10/501,698. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JON P. WEBER can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Satyendra K. Singh/
Examiner, Art Unit 1657

/JON P WEBER/
Supervisory Patent Examiner, Art Unit 1657